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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
BAUSCH, SARAE L	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 11/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/073,464	TIEDJE ET AL.	
	Examiner	Art Unit	
	Sarae Bausch	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. In view of the appeal brief filed on 08/30/2006, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

2. Currently, claims 1-6 and 9-14 are pending in the instant application. Claims 7 and 15-21 have been canceled. All the amendments and arguments have been thoroughly reviewed but were found insufficient to place the instantly examined claims in condition for allowance. The following rejections are either newly presented or are reiterated from the previous office action. Any rejections not reiterated in this action have been withdrawn. **This action is Non-final.**

New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 3 and 11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 and 11 is rejected as vague and indefinite because the claim fails to further limit claim 1 and 9, respectively. Claim 3 and 11 recite wherein said test bacteria are pathogenic organisms however, pathogenic organisms are a broader class of species than bacteria. Therefore, claim 3 and 11 fail to further limit claims 1 and 9, respectively.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

6. Claims 1-6 and 8-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Hogan et al. (US Patent 6821770 filing date 03/03/1999)

With regard to claim 1, 5 and 9, Hogan et al. teach a method identifying bacteria by hybridizing a released polynucleotides from a biological sample to a probe matrix. Hogan et al. teach the released polynucleotides are amplified prior to hybridization (see column 6, lines 44-60). Hogan et al. teach the probe matrix includes probes arrayed on a testing device where each locus specifically hybridizes nucleic acid from one or a plurality of microorganisms species (see column 11, lines 1-13). Hogan et al. teach a preferred collection of species probes would be E. coli, Staphylocoous aureus, Candida albican, Pseuomonas aeruginosa, and Streptococcus pneumoniae (reference DNA from four strains of reference bacteria) (see column 30, lines 14-20). Hogan et al. teach labeling of probes and polynucleotides with fluorescent labels that produce light at different wavelengths (see column 36, lines 40-45). Hogan et al. teach a plurality of nucleic acid probes are physically combined at a single locus in a testing device (see column 29, lines 24-32) and teach identification of bacteria is determined by hybridization of the sample to the testing format, which includes a DNA chip (claim 5) (see column 36, lines 1-10). Hogan et al. teach calculating the hybridization signal to determine the identity of the bacteria (see column 37, lines 5-25).

With regard to claim 2-3 and 10-11, Hogan et al. teach rapid clinical diagnosis of microbial infection including infections of the oral cavity, blood, urinary tract which include samples obtained from subjects (see column 13, lines 38-50).

With regard to claim 4 and 12, Hogan et al. teach identification of one or more microbes in environmental samples (see column 13, lines 58-62).

With regard to claim 6 and 14, Hogan et al. teach an algorithm that correlates the profile of the hybridization data with identities of organisms and performs a quantitative analysis to

provide a basis for determining whether a numerical result from a hybridization procedure is positive or negative (see column 38, lines 8-28) and teaches normalization of the hybridization data (see column 44, lines 20-24) (calculating a statistical analysis).

With regard to claim 13, Hogan et al. teach producing hybridization profiles of the probe matrix hybridization (hybridization profile of test and reference bacteria) (see column 37, lines 5-24).

7. Claims 1-6 and 8-14 are rejected under 35 U.S.C. 102(e) as being anticipated by Gingeras et al. (US Patent 6228575 filed 02/07/1997).

With regard to claim 1 and 9, Gingeras et al. teach a method of oligonucleotide array for speculating and phenotyping organism by providing an array of known locations on a substrate comprising a plurality probes to reference DNA sequences hybridizing target nucleic acid sequence to array and based on hybridization pattern identifying the genotype of the first organisms(see column 3, lines 1-13 and column 4, lines 7-13). Gingeras et al. teach amplification of nucleic acid sample prior to hybridization (See column 8, lines 34-37) (providing amplified genomic sequences). Gingeras et al. teach hybridized nucleic acid are detected by detecting one or more labels attached to the sample nucleic acids and include fluorescein labels (see column 8, lines 46-57) (labeled DNA with a fluorescent dye). Gingeras et al. teach the screening method allows one to build up a data base of hybridization patterns corresponding to different species. Gingeras et al. teach identifying mycobacterium species by measuring fingerprint data (hybridization pattern on array) (see column 30, lines 65-67) by a collection of samples and based on these measurements a systematic way to predict species of each member of the collect by comparing the signal produced by the target at each hybridization

site compared to the signal produced by Mt rpoB (see column 31, lines 1-5). Specifically, Gingeras et al. teach hybridization analysis of 7 mycobacteria species (reference samples) and teach that a reference sequence can be sequence of nucleotides, DNA (see column 12, lines 51-53 and column 34, lines 45-51). Gingeras et al. teach fluorescently labeled amplicons from mycobacteria species hybridized to a DNA chip and comparing the hybridization pattern to amplicons hybridized to the DNA chip from M. tuberculosis (test bacteria) (see column 35, lines 15-25 and table 4). Gingeras et al. teach analyzing the fingerprint pattern of each species followed by classification analysis (calculating the hybridized DNA fluorescent dye signal and reference DNA fluorescence to determine identity) (See column 36, lines 35-51).

With regard to claim 2-3 and 10-11, Gingeras et al. teach assaying biological samples, which refers to a sample obtained from an organism or clinical sample from a patient (See column 8, lines 22-34).

With regard to claim 4 and 12, Gingeras et al. teach assaying biological samples obtained from an organism (environmental sample) (see column 8, lines 22-25).

With regard to claim 6, 13, and 14, Gingeras et al. teach hybridization patterns (producing hybridization profiles) correlated to species determination using mathematical pattern recognition algorithms (calculating by statistical analysis) (see column 30, lines 5-67 and column 31, lines 1-67).

Maintained Rejection

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-5, 8-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuiper et al. (Current Opinion in Biotechnology, 1999, 10:511-516) and Greisen et al. (J.Clin. Microbial. 1994, vol. 32, pp 335-351). It is noted that this rejection was previously presented in section 6 of the previous office action mailed 07/01/2005 and has been maintained for reasons of record in the previous office action and is reiterated below.

Kuiper et al. teaches producing a specific DNA array for the rapid identification of pathogens and spoilage bacteria (instant claim 3-4, 11-12) (see page 512, 2nd column, 2nd paragraph). Kuiper et al. teaches producing microarrays by spotting amplicon of each ORF annotated in the genome sequence of interest on a defined support material, preferably glass-slides. Kuiper et al. teaches fluorescently labeled cDNA is used for hybridization to the DNA arrays and signal detection by confocal laser scanning (instant claim 7 and 11) (see page 512, 2nd column, 1st paragraph). Kuiper further exemplifies that different cDNA strains can be differentially labeled and used in one combined sample for hybridization providing the possibility of multiplexing and allowing for several different cDNA samples (see page 512, 2nd column, 1st paragraph). Kuiper et al. does not teach the use of at least four strains of reference bacterial species.

Greisen et al. teaches a method of detecting DNA for the identification of over 60 different strains representing 18 different bacterial species found as pathogens (instant claim 3 and 11) or presumptive contaminants in human CSF (see page 336, 1st column, 1st paragraph).

Greisen et al. exemplifies amplifying DNA, followed by gel electrophoresis of amplified products, and blotting the gel onto a Pall Biodyne membrane and fixing the DNA to the membrane by a UV crosslinker (amplified genomic DNA arrayed on a solid support, microchip) (instant claim 5) (see page 336, 1st column, last paragraph cont'd to 2nd column). Greisen et al. teach probes of target DNA and reference DNA labeled with ^{32}P (see probe hybridization, page 338 and table 3) and hybridization of target DNA probes and reference DNA probes hybridized to DNA blots in 5xSSPE. Greisen et al. teach up to 12 meningitis and contaminant probes (reference and test DNA) tested against seven major bacterial species causing meningitis and identification of bacteria in CSF based on the hybridization pattern of each probe (instant claim 8 and 13) (see page 346, 2nd column, last two paragraph and table 4). Greisen et al. teaches that the use of the panel of probes would enable a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples (see page 350, 1st column, last paragraph). Greisen et al. does not teach co-hybridizing target and reference DNA in a single step or the use of fluorescence detection for hybridization.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have improved the method of identification of pathogens using fluorescently labeled cDNA probes as taught by Kuiper et al. to include the testing of at least seven bacterial species causing meningitis by using up to 12 meningitis and contaminant probes as taught by Greisen et al. The ordinary artisan would have been motivated to use multiple probes, comprising up to 12 meningitis and contaminant probes as taught by Gresien et al. in the DNA microarray method taught by Kuiper et al. because Kuiper et al. suggests using different cDNA strains differentially labeled to be used in one combined sample for hybridization.

Furthermore, the ordinary artisan would have had a reasonable expectation of success that using up to 12 different probes to test against seven major bacterial species that cause meningitis could be used in the method of Kuiper et al. because Kuiper et al. suggests using different cDNA strains in one sample for multiplexing and allowing for analysis of several different cDNA samples at one time.

Furthermore, it would have been prima facie obvious to improve the method of detection of bacteria in a sample using southern blot hybridization as taught by Greisen et al. to include co hybridization of probes in one combined sample and fluorescence detection hybridization as taught by Kuiper et al. The ordinary artisan would have been motivated to improve the method of the southern blot hybridization method as taught by Greisen et al. to include a more rapid, automated method of multiplexing for the identification of pathogens in bacteria as taught by Kuiper et al. because Kuiper et al. suggests using different multiple labeled probes for combining several different cDNA sample for the possibility of multiplexing. Furthermore, the ordinary artisan would be motivated to use fluorescent-labeled probes to eliminate the use of radioactivity, as fluorescence in non-radioactive. The ordinary artisan would have had a reasonable expectation of success that the use of fluorescent-labeled probes to detect pathogens could be used in the method of Greisen et al. because Kuiper et al. teach the use of fluorescent-labeled probes hybridizing to a sample for the detection of pathogens. The ordinary artisan would have had a reasonable expectation of success that the use of co hybridizing probes in a single step could be used in the method of Greisen et al. because Greisen et al. teaches the use of panel of probes that would enable the use of a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples.

Response to Arguments

10. The response filed 08/30/2005 traverses this rejection. Attorneys arguments have been fully considered but are not persuasive for the reasons that follow.

The response assert that there is no motivation to combine the art. The response state that the general consensus in the art that one having ordinary skill in the art would not use a reference based upon 16S rRNA universal primers to create the response's hybridization method to identify bacteria. This response has been thoroughly reviewed but not found persuasive.

The specification states that the art-recognized disadvantages to the 16S rRNA gene detection methods is that the molecule is too conserved to provide good resolution at the species and subspecies level. However, is it noted that the claims are not drawn to providing resolution at the species and subspecies levels. The claims only require identification of a bacteria among different reference species of bacteria. The claims do not require identification of the subspecies of bacteria or species, the claims only require identification of "a bacteria". Furthermore, Greisen et al. teach the detection and identification of a wide range of bacterial pathogens using universal PCR primers of 16S rRNA (see page 335, 2nd column, last paragraph) and teach identification of over 60 different strains representing 18 different bacterial species found as pathogens or presumptive contaminants in human CSF (see page 336, 1st column, 1st paragraph).

The response assert that Kuipers teaches using a single bacterial species when suggesting that arrays might be useful to compare relative gene transcription rates and does not suggest that using a plurality of bacterial species would be advantageous. This response has been thoroughly reviewed but not found persuasive. The claims are not drawn to comparing relative gene transcription rates the claims are drawn to method of identification of bacteria based on

hybridization of target and reference DNA. Furthermore, the response do not provide a citation where Kuipers et al. teach that it would be deleterious to use a multi-species array. Furthermore, Kuiper exemplifies that different cDNA strains can be differentially labeled and used in one combined sample for hybridization providing the possibility of multiplexing and allowing for several different cDNA samples (see page 512, 2nd column, 1st paragraph).

The response asserts on page 11, that the examiner has not taught every element of the claimed invention and asserts that Kuipers et al. states that such DNA bacterial identification arrays are unavailable in the art. The response points to column 2, 2nd paragraph, page 512. This response has been thoroughly reviewed but not found persuasive. Kuipers, in its entirety, teaches DNA microarray analysis of wild type and mutant strain cDNAs by differentially labeling and combining the sample for hybridization and multiplexing (see column 2, 1st paragraph, page 512) and further teaches that specific DNA microarrays can be developed for rapid identification of pathogens and spoilage bacteria. The response further that well settled patent law states that an invention is not obvious where the prior art gives no direction as to which of many possible choices is likely to be successful. In the instant case, Kuipers et al. teach that fluorescently labeled DNA from two different samples is successful for analysis of DNA hybridization and distinguishing (identifying) mutant and wild type strains and Kuipers et al. further teaches that DNA microarray analysis can be developed for rapid identification of pathogens. Therefore Kuipers and Greissen teach that identification of bacteria by detection of hybridization of multiple references species can be identification by DNA microarray analysis of fluorescently labeled probes and give direction as to which choice will be successful.

The response asserts on page 12, that the examiner has not pointed to any teachings within Kuipers that provides any teachings regarding which bacterial genomes should be utilized, what kind of fluorescent DNA labels are optimum, or how to calculate the data once the fluorescent signals are detected in order to identify any bacterial species. This response has been thoroughly reviewed but not found persuasive. The claims are not drawn to identifying specific bacterial genomes, fluorescent labels or how the data is calculated. The claims are broadly drawn to providing amplified genomic sequences, labeled target DNA with a fluorescent dye, labeled reference DNA with a fluorescent dye, and calculating the hybridized target fluorescent signal and reference fluorescent signal. Kuipers et al. teaches multiplexing of hybridization by fluorescently labeled cDNA and detecting the signals by confocal laser scanning (calculating hybridization signal) and furthermore Kuipers et al. teaches differentially labeling two difference cDNA strains. Kuipers et al. and Grissen et al. teach the claimed invention. In response to applicants arguments that Kuiper et al. nor Greisen disclose the claimed invention, Kuiper et al. teach spotting amplicons of open reading frames in the genome sequence of interest on a defined support material and teach that over 100,000 spots can be accommodated on glass slides providing sufficient combinatorial possibilities for bacterial genome application (see page 512, 2nd column, 1st full paragraph). Kuiper further teaches differentially fluorescent-labeled wild type and mutant cDNA to allow for multiplexing. As stated in the rejection of record, Kuiper et al. does not teach the use of at least four strains of reference bacterial species, however Kuiper et al. in view of Greisen et al. does teach modifying the method of using differentially labeled cDNA probes on a microarray as taught by Kuiper to include 12 different probes of seven

reference bacterial species, as taught by Greisen to test for at least seven bacterial species causing meningitis. Therefore, Kuiper et al. and Greisen et al. teach the claimed invention.

The response asserts that futuristic tone set by Kuipers passage and Kuipers is not concluding that these types of microorganism identification methods are already present in the art. Kuipers et al. teach identification of two different bacterial strains (wild type and mutant strains) by differential labeling and multiplexing by DNA microarray and hybridization analysis (see column 2, 1st paragraph, page 512). The examiner is not relying on the passage that applicant has pointed to anticipate the claimed invention. The examiner is asserting that there is an expectation of success that the method could be used to multiplex several different strains of bacteria because Kuiper et al. states that they will be developed.

The response asserts that Kuipers was not discussing the possibility of identifying bacterial species but detecting gene transcription levels from a single bacterial species by comparing wild type and mutant strain cDNA. The response states that Kuiper et al. does not teach identification of any bacterial strains based upon hybridizing labeled fluorescent reference DNA from at least four strains of reference bacteria and fluorescently labeled target DNA. This response has been thoroughly reviewed but not found persuasive. The claims do not require identification of bacterial strains. The claims only require identification of "a bacteria" and Kuipers et al. and Grissen et al. teach a method of identification of a bacteria by labeled target DNA and labeled reference DNA from four different strains and hybridizing the target and reference DNA.

The response asserts that the examiner has not pointed to Greisens for any teaching except "12 different probes of seven reference bacterial species" and consequently Greisens et al. does not teach any methods for identifying bacterial strains based upon hybridizing labeled fluorescent reference and labeled fluorescent target DNA. This response has been thoroughly reviewed but not found persuasive. Examiner did not point to Greisen for only "12 different probes of seven reference bacterial species", Examiner stated Greisen et al. teaches a method of detecting DNA for the identification of over 60 different strains representing 18 different bacterial species found as pathogens (instant claim 3 and 11) or presumptive contaminants in human CSF (see page 336, 1st column, 1st paragraph). Greisen et al. exemplifies amplifying DNA, followed by gel electrophoresis of amplified products, and blotting the gel onto a Pall Biodyne membrane and fixing the DNA to the membrane by a UV crosslinker (amplified genomic DNA arrayed on a solid support, microchip) (instant claim 5) (see page 336, 1st column, last paragraph cont'd to 2nd column). Greisen et al. teach probes of target DNA and reference DNA labeled with ^{32}P (see probe hybridization, page 338 and table 3) and hybridization of target DNA probes and reference DNA probes hybridized to DNA blots in 5xSSPE. Greisen et al. teach up to 12 meningitis and contaminant probes (reference and test DNA) tested against seven major bacterial species causing meningitis and identification of bacteria in CSF based on the hybridization pattern of each probe (instant claim 8 and 13) (see page 346, 2nd column, last two paragraph and table 4). Greisen et al. teaches that the use of the panel of probes would enable a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples (see page 350, 1st column, last paragraph). Greisen et al. does not teach co-hybridizing target and reference DNA in a single

step or the use of fluorescence detection for hybridization. As stated in the office action mailed 07/01/2005, it would have been prima facie obvious to improve the method of detection of bacteria in a sample using southern blot hybridization as taught by Greisen et al. to include co hybridization of probes in one combined sample and fluorescence detection hybridization as taught by Kuiper et al. The ordinary artisan would have been motivated to improve the method of the southern blot hybridization method as taught by Greisen et al. to include a more rapid, automated method of multiplexing for the identification of pathogens in bacteria as taught by Kuiper et al. because Kuiper et al. suggests using different multiple labeled probes for combining several different cDNA sample for the possibility of multiplexing. Furthermore, the ordinary artisan would be motivated to use fluorescent-labeled probes to eliminate the use of radioactivity, as fluorescence in non-radioactive. The ordinary artisan would have had a reasonable expectation of success that the use of fluorescent-labeled probes to detect pathogens could be used in the method of Greisen et al. because Kuiper et al. teach the use of fluorescent-labeled probes hybridizing to a sample for the detection of pathogens. The ordinary artisan would have had a reasonable expectation of success that the use of co hybridizing probes in a single step could be used in the method of Greisen et al. because Greisen et al. teaches the use of panel of probes that would enable the use of a single CSF sample to obtain multiple probe hybridization results and form a more rapid and sensitive means of detecting bacteria in clinical samples. Therefore Kuiper et al. and Greisen et al. teach the claimed invention.

The response asserts that examiner has not pointed to where Kuipers or Greisen teaches the limitations of claims 2-5 and 10-12. This response has been thoroughly reviewed but not found persuasive. See section 9 above.

The response asserts on page 15 that the examiner has simply offered personal interpretations of passages within the cited art and is not sported by any explicit statements within the cited art. This response has been thoroughly reviewed but found persuasive. Kuiper et al. does suggest using DNA chip analysis for the identification of multiple bacterial species (see column 2, 2nd para: page 512 and figure 1) therefore there is an expectation of success that the DNA hybridization and array analysis taught by Kuipers et al. could be used in identification of bacterial species as taught by Greissen et al.

11. Claims 6 and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuiper et al. (Current Opinion in Biotechnology, 1999, 10:511-516) and Greisen et al. (J.Clin. Microbial. 1994, vol. 32, pp 335-351) as applied to claims 1-5, 7-13, and 15 above, and further in view of Arfin et al.. (J. Biol. Chem. 2000, vol. 275, pp. 29672-29684). This rejection was previously presented in section 7 of the previous office action mailed 07/01/2005 and is reiterated below.

The method of Kuiper et al. and Greisen et al. is set forth in section 6 above. Kuiper et al. and Greisen et al. do no teach statistical analysis in calculating the target signal to reference signal hybridization ratio at each array element.

Arfin et al. teach replication and appropriate statistical analysis is required for determining the accuracy of DNA microarray measurements. Arfin et al. teach that thousands of measurements are obtained from a single experiment using DNA microarrays experiments and in order to interrupt data from experiments it is necessary to employ statistical methods capable of distinguishing chance occurrences from biologically meaningful data (see page 29676, 1st column, last paragraph). Arfin et al. teach using a t test to evaluate the difference between the

means of two groups employing the variance within groups as an error term. Arfin et al. teach using the t test to determine statistical differences among different filters hybridized with the same RNA of the same genotype as well as differences among different RNA preparations of the same genotype hybridized to the same filters (see page 29674, 2nd column, 3rd paragraph).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the method of Kuiper et al. and Greisen et al. of identifying bacteria using a microarray to include statistical analysis of the data as taught by Arfin et al. The ordinary artisan would have been motivated to improve the method of Kuiper et al. and Greisen et al. to include statistical analysis of the data obtained by the microarray analysis because Arfin et al. teach replication and appropriate statistical analysis is required for determining the accuracy of DNA microarray measurements. Furthermore Arfin et al. teach that thousands of measurements are obtained from a single experiment using DNA microarrays experiments and in order to interrupt data from experiments it is necessary to employ statistical methods capable of distinguishing chance occurrences from biologically meaningful data, therefore, the ordinary artisan would have had a reasonable expectation of success of using statistical data analysis in the method of Kuiper et al. and Greisen et.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Response to Arguments

12. The response traverses the rejection on pages 16-18 mailed 08/30/2006. These arguments have been thoroughly reviewed but not found persuasive for the following reasons:

The response asserts that the examiner has mischaracterized the Arfin et al. reference and

assert that the Arfin reference does not suggest that this statistical analysis could be used to calculate an expression profile from a fluorescently labeled reference and target DNA. This response has been thoroughly reviewed but not found persuasive. Arfin et al. does teach statistical analysis of data generated by gene expression profiling experiments (See page 29673, 2nd column, 1st paragraph).

The response asserts on page 18, Arfin et al. does not suggest that more than one bacterial species could be arrayed and asserts that Arfin et al. teach arrays limited to E. Coli. It is noted that Arfin was not cited to teach the method of identifying a bacteria but to teach the step of statistical analysis of the DNA hybridization array data.

The response asserts that there is no expectation of success that Arfin et al. could be used to calculate data from fluorescently labeled reference and target DNA. The response further asserts that the examiner offers personal interpretation of passages. It is noted that the passage the response is relying upon is not a personal interpretation and is taught by Arfin that thousand of measurements are obtained from a single experiment using DNA microarray experiments and in order to interpret data from experiments it is necessary to employ statistical methods capable of distinguishing chance occurrences from biologically meaningful data (see page 29676, 1st column, last paragraph). Therefore the ordinary artisan would have had a reasonable expectation of success when generating data from the DNA hybridization array taught by Griessen and Kuiper that statistical analysis would distinguish chance occurrences from biologically meaningful data.

For these reasons, and the reasons made of record in the previous office actions, the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sarae Bausch whose telephone number is (571) 272-2912. The examiner can normally be reached on M-F 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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